Journal of the American College of Cardiology
© 2002 by the American College of Cardiology Foundation
Published by Elsevier Science Inc.

Vol. 39, No. 5, 2002
ISSN 0735-1097/02/$22.00
PII S0735-1097(02)01686-8

Valve Disease

A Prognostic Model for Predicting the Disappearance of Left Atrial Thrombi Among Candidates for Percutaneous Transvenous Mitral Commissurotomy

Songkwan Silaruks, MD,* Bandit Thinkhamrop, PHD,† Wirote Tantikosum, MD,* Chaiyasith Wongvipaporn, MD,* Pyatat Tatsanavivat, MD,* Virat Klungboonkrong, MD, FACC*
Khon Kaen, Thailand

OBJECTIVES We sought to develop a prognostic model to predict the disappearance of left atrial thrombi (LAT) among candidates for percutaneous transvenous mitral commissurotomy (PTMC).

BACKGROUND Complete LAT resolution can be achieved with oral anticoagulation, allowing a number of patients to safely undergo PTMC.

METHODS We randomly allocated 108 PTMC candidates with LAT into two subsets—one to derive the model and the other to validate it. The existence of LAT and its size were measured by transesophageal echocardiography. Patients were given oral anticoagulation and followed up for 6 to 34 months. There was a 62% disappearance rate of LAT.

RESULTS We developed the following model: P = 1/(1 + exponential [−8.1 + 1.8 NYHA + 0.7 area]), where NYHA = New York Heart Association functional class (from I to IV), and area = LAT area (in cm^2). The model was well calibrated (goodness-of-fit test, p = 0.82) and well discriminated (area under the receiver-operating characteristics [ROC] curve = 0.92). Performance in the validating sample was equally good (area under the ROC curve = 0.94; goodness-of-fit test, p = 0.16). When a cut-off point of p > 0.7 was used to designate the LAT disappearance in the validating set, the model had a sensitivity, specificity and positive and negative predictive values of 93.3%, 79.2%, 84.9% and 90.5%, respectively.

CONCLUSIONS Combined clinical (NYHA functional class) and echocardiographic (LAT area) variables are predictive of the 34-month outcome of oral anticoagulation for LAT resolution among PTMC candidates. This simple and highly predictive model might be potentially useful for clinical assessment and proper management. (J Am Coll Cardiol 2002;39:886–91) © 2002 by the American College of Cardiology Foundation

Percutaneous transvenous mitral commissurotomy (PTMC) has been used successfully as an alternative to surgical treatment in patients with symptomatic, severe mitral stenosis, particularly when regurgitation and valvular calcifications are limited (1–10). The presence of a left atrial thrombus (LAT) is generally considered a contraindication to this procedure, because of embolic risk, which may arise when catheters and wires are manipulated in the left atrium (1–3,8). Recent reports have demonstrated that, in some circumstances, complete resolution of LAT can be achieved with oral anticoagulant therapy, allowing patients to undergo PTMC safely (11–15). However, to date, no study has attempted to develop a prognostic model to predict such success. A model would be particularly useful in developing countries, where surgical treatment is relatively expensive and unable to meet the demand. Knowing the likelihood of LAT disappearance would help the physician decide whether to proceed with surgical repair or to continue oral anticoagulation until LAT resolution and then to perform PTMC.

The purpose of our study was to develop and validate a simple model to predict the likelihood of LAT disappearance among PTMC candidates receiving long-term oral anticoagulant therapy.

METHODS

Study group. Our prospective cohort study was conducted at Khon Kaen University Hospital between August 1996 and October 2000. All patients with mitral stenosis who were candidates for PTMC were consecutively recruited. The candidates had symptomatic (16), severe mitral stenosis, with a total echocardiographic score of ≤11 for the mitral valve and a mitral regurgitation score of ≤2+ (17). Both transthoracic echocardiography (TTE) and multiplane transesophageal echocardiography (TEE) were performed in all patients before PTMC. Patients receiving an oral anticoagulant more than 72 h previously or who had a contraindication to TEE were excluded.

Echocardiographic method and variables. Standard TTE and multiplane TEE studies (18) were performed using a color Doppler system (2.5 or 3.5 MHz) and multiplane transducer (5.0-MHz; Hewlett-Packard Imaging System

From the *Department of Medicine, Faculty of Medicine, and †Department of Biostatistics and Demography, Faculty of Public Health, Khon Kaen University, Khon Kaen, Thailand. This paper was presented as an abstract form at the 50th Annual Scientific Sessions of the American College of Cardiology in Orlando, Florida on March 18–21, 2001.

Manuscript received August 14, 2001; revised manuscript received November 28, 2001, accepted December 14, 2001.

Abbreviations and Acronyms

CI = confidence interval
INR = international normalized ratio
LASEC = left atrial spontaneous echo contrast
LAT = left atrial thrombus
NYHA = New York Heart Association
PTMC = percutaneous transvenous mitral commissurotomy
ROC = receiver-operating characteristics
TEE = transesophageal echocardiography
TTE = transthoracic echocardiography

Sonos 1000 and since August 1999, 5000), respectively. Transesophageal echocardiography was performed within 24 h of the TTE study by echocardiographers who were unaware of the TTE findings. Left atrial thrombus was diagnosed according to the presence of an intracavitary echogenic mass clearly distinct from the left atrial endocardium and the pectinate muscles, and it was visualized on at least two different planes (18). The maximal area of LAT was measured by planimetry utilizing the built-in echocardiographic system's software. Left atrial spontaneous echo contrast (LASEC) was characterized by dynamic clouds of echoes within the left atrial cavity. The severity of LASEC was graded from 0 to 4+, as described by Fatkin et al. (19). The observation of LASEC was standardized by varying both the gain and compress settings throughout their full range during each study. We measured left atrial diameter at the end of systole (from the parasternal view), mitral valve area (by both planimetry from two-dimensional echocardiography and the continuous wave Doppler pressure half-time method) and the mitral valve echocardiographic score (17).

Both TTE and TEE findings were recorded on VHS videotape for subsequent review to identify LAT and LASEC and to determine the maximal area and mobility of the LAT. All echocardiographic measurements were done independently by three echocardiographers. Any differences among them regarding the recognition of either LAT or LASEC were resolved by consensus. Written, informed consent was obtained from each patient, and the research protocol was approved by our institutional Ethics Committee.

Left atrial thrombi were detected by TEE in all 108 patients (in the left atrial appendage of all patients and in the left atrial body of 15 patients) and by TTE in only 18 patients. Transesophageal echocardiography revealed LASEC in all 108 patients, whereas TTE could detect LASEC in only 16.

Management of the patients. After identification of LAT, all patients were given oral anticoagulant therapy, maintaining the therapeutic range of the international normalized ratio (INR) of 2.0 to 3.0 (20). The outcome of LAT was serially studied using both TTE and TEE after the first six months and subsequently, depending on the clinical indications, until complete resolution of LAT or just before mitral valve surgery. Percutaneous transvenous mitral commissurotomy was performed as soon as possible after complete resolution of LAT.

Statistical analysis. We randomly allocated the 108 subjects into two subsets of 54 each—the training set and the validating set. Identification of candidate variables was based only on the 37 outcomes of the training set. Independent variables for the model were identified prospectively to avoid increased risk of type I errors. Initially, predictors of LAT resolution were identified by the investigators; then the effect of each potential predictor was examined using univariate logistic regression. To avoid over-fitting the predictive model, we limited the number of candidate variables in the initial model to four, based on the size of the study group and the number of outcomes (21), as well as on the strength of the relationship to LAT disappearance obtained in the univariate analysis, data availability before oral anticoagulant therapy and fewer measurement errors in practice.

We applied methods for development of prognostic models used by Kleinbaum et al. (22) and Hosmer and Lemeshow (23). Continuous variables were tested for the linear relationship assumption, using a restricted cubic spline allowing three knots (24). Because there was no departure from linearity, the variables were entered in their original form. Model fitting was done using backward elimination; the variables were removed, one at a time, if the p value of the likelihood ratio test was >0.05. The adequacy of the model and testing of goodness-of-fit were examined according to Hosmer and Lemeshow (23). Once the final model was obtained, the receiver-operating characteristics (ROC) curve (25) was constructed. The area under the ROC curve and its 95% confidence interval (CI) were then estimated.

The model was presented as a logistic function: $P = 1/(1 + \text{Exp}[-(\alpha + \beta X)])$, where α refers to the constant and β is the coefficient to be estimated. P was the probability of LAT resolution, which can also be viewed as the risk score, and X was the predictor. Exp was the exponential function (raising the natural log to the $[-(\alpha + \beta X)]$ power) (23). From the ROC curve, the optimal cut-off point was determined, which is the value of P that maximizes both the sensitivity and specificity of the model.

The model was validated using the validating set. The ROC curve was reconstructed, and the area under the ROC curve and its 95% CI were estimated. Testing for the equality of the area under the two ROC curves was performed according to Cleves (26). The diagnostic performance of the model for sensitivity, specificity and positive and negative predictive values was estimated together with their 95% CIs. All analyses were performed using STATA, version 6 (StataCorp, College Station, Texas). A nomogram was constructed based on the model and the range of values of all variables in the model.

Table 1. Baseline Characteristics of Patients in the Training Set (n = 54)

Variables	
Age (yrs)	40.0 ± 7.7
Atrial fibrillation	21 (38.9%)
Left atrial end-systolic dimension (mm)	5.2 ± 0.7
Mitral valve area (cm^2)	0.8 ± 0.2
Pressure half-time (mm Hg)	323.3 ± 71.7
Left atrial thrombus area (cm^2)	2.26 ± 1.0
Total mitral valve echocardiographic score	7.4 ± 1.3
Mean PG across mitral valve (mm Hg)	12.7 ± 3.2
Tricuspid regurgitation PG (mm Hg)	41.5 ± 17.7
LASEC on TEE grade	
1+	13 (24.1%)
2+	22 (40.7%)
3+	11 (20.4%)
4+	8 (14.8%)

Data are presented as the mean value ± SD or number (%) of patients.
LASEC = left atrial spontaneous echo contrast; PG = pressure gradient; TEE = transesophageal echocardiography.

RESULTS

Total patients and magnitude of the outcome. Among a total of 494 consecutive patients with symptomatic, severe mitral stenosis, 379 were candidates for PTMC. Among these PTMC candidates, 108 with documented LAT comprised the study cohort (age range 19 to 60 years; mean [±SD] 40.1 ± 7.6 years). The duration of follow-up ranged from 6 to 34 months (mean [±SD] 12.2 ± 6.2 months; median 11 months). A total of 1,209 patient-months were observed. Complete resolution of LAT was demonstrated in 67 patients (62%), with an overall thrombus disappearance rate of 5.25 per 100 patient-months under observation (95% CI 3.96 to 6.97) or 63.0 per 100 patients per year (95% CI 47.5 to 83.6). All 67 patients subsequently underwent PTMC successfully. There were no procedure-related complications during or immediately after PTMC. None of the patients with LAT in the atrial body (n = 15) had LAT resolution, so all of them underwent mitral valve surgery.

None of our patients was receiving oral anticoagulant therapy before the study.

There were 26 systemic embolic events (2.1 per 100 patient-months) before study entry, but none of these patients developed a clinical embolism after starting oral anticoagulant therapy. During follow-up, the only bleeding complication was minor (n = 11).

Table 2. Univariate Logistic Regression: Unadjusted OR of Each Clinical Variable in Relation to Resolution of LAT

Variables	n	LAT Disappearance (%)	OR	95% CI	p Value
Age (one-year increase)	54	NA	1.04	0.96–1.12	0.369
Gender					0.623
Male	19	63.2	1.00		
Female	35	71.4	1.46	0.45–4.77	
Syncope					0.568
Yes	5	80.0	1.94	0.20–18.79	
No	49	67.3	1.00		
Stroke					0.406
Yes	15	60.0	1.00		
No	39	71.8	1.70	0.49–5.90	
NYHA functional class (one-class increase)	54		0.10	0.03–0.37	0.001
Atrial fibrillation					0.038
Yes	21	85.7	4.4	1.1–18.0	
No	33	57.6	1.00		

CI = confidence interval; LAT = left atrial thrombus; NA = not applicable; NYHA = New York Heart Association; OR = odds ratio.

Patient characteristics of the training set. Of 54 patients in this set, the LAT completely resolved in 37 (68.5%). The follow-up duration ranged from 6 to 28 months (median 10.5 months). The patients' age ranged from 19 to 60 years (mean [±SD] 40.0 ± 7.7 years). Approximately two-thirds of the patients were female. The baseline clinical and echocardiographic characteristics are summarized in Table 1.

Development of the prognostic model. Fourteen potential predictors of LAT resolution were prospectively specified. However, the data in our training set allowed for only 11 of them to be examined for their effects in the univariate logistic regression (Tables 2 and 3). The effects of the remaining three variables (including LASEC, mitral valve area and pressure half-time) were not examined, because of the small sample size.

Among the 11 variables, five were statistically significant with respect to the outcome ($p < 0.05$). These included: 1) the presence of atrial fibrillation; 2) New York Heart Association (NYHA) functional class; 3) mitral valve score; 4) left atrial size; and 5) LAT area. We discarded the mitral valve score, because its measurement was prone to error in practice. Thus, four candidate variables remained for the initial multivariable model (Table 4). However, the effects

Table 3. Univariate Logistic Regression: Unadjusted OR of Each Echocardiographic Variable in Relation to Resolution of LAT

Variables	n	LAT Disappearance (%)	OR	95% CI	p Value
Aortic regurgitation					0.785
Yes	40	67.5	1.00		
No	14	71.4	1.20	0.32–4.57	
Mitral valve score (one-score increase)	54	NA	0.20	0.08–0.53	0.001
Mean pressure gradient (one-unit increase)	54	NA	0.95	0.79–1.14	0.593
Left atrial size (1-cm increase)	54	NA	0.28	0.10–0.79	0.017
LAT area (1-cm^2 increase)	54	NA	0.44	0.29–0.69	<0.001

Abbreviations as in Table 2.

Table 4. The Initial Multivariable Logistic Regression Model: OR of Each Variable, Adjusted for Effects of All Other Varibles in Relation to Resolution of LAT

Variables	Coefficient	Standard Error	OR	95% CI	p Value
NYHA (one-class increase)	−1.8611	0.7641	0.15	0.03–0.69	0.015
LAT area (1-cm^2 increase)	−0.6467	0.2530	0.52	0.32–0.86	0.011
Atrial fibrillation	0.8981	0.9508	2.45	0.38–15.83	0.345
Left atrial size (1-cm increase)	−0.0942	0.7740	0.91	0.20–4.15	0.903
Constant	8.2668	4.4564	—	—	—

Abbreviations as in Table 2.

of atrial fibrillation and left atrial size turned out to be nonsignificant, and these two variables were removed from the initial model, without any effect on the model (likelihood ratio test, p = 0.961 and 0.941, respectively). Thus, the final model obtained (Table 5) can be written as:

$$P = 1/(1 + \text{Exp}[-8.0827 + 1.8012\ \text{NYHA} + 0.7028\ \text{area}])$$

Model predictive capability. The area under the ROC curve of the final model was 0.92 (95% CI 0.85 to 0.99) (Fig. 1a). The model fits the data well (goodness-of-fit test, p = 0.82). The model was simplified to:

$$P = 1/(1 + \text{Exp}[-8.1 + 1.8\ \text{NYHA} + 0.7\ \text{area}])$$

where P = probability of LAT resolution; NYHA = New York Heart Association functional class (from I to IV); and area = area of the LAT (cm^2).

Adequacy of the model. Standard residuals and measures of influence for the logistic regression were calculated to examine the individual effect of each patient on the model; none was found to influence it.

Validation of the model. The validating set of 54 patients was used to validate the model. The baseline characteristics of the patients were similar to those of the training set. The LAT completely disappeared in 30 patients (55.6%).

The area under the ROC curve was 0.94 (95% CI 0.90 to 1.00) (Fig. 1b). The performance of the model in the validating sample was not significantly different from that of the training set (p = 0.462). The model fits the data well (goodness-of-fit test, p = 0.16). The optimal cut-off point of P, as suggested by the ROC curve, was 0.7.

Assessing the diagnostic performance of the model. The performance of the model was tested against the validating set by substituting the true NYHA functional class and LAT area of each patient into the model to obtain P. We used a cut-off point of P > 0.7 to designate the disappearance of LAT, and then we compared the outcome predicted by the model (diagnostic test) with the true outcome (reference standard). The model had a sensitivity of 93.3% (95% CI 77.9% to 99.2%), specificity of 79.2% (95% CI 57.8% to 99.9%), positive predictive value of 84.9% (95% CI 68.1% to 94.9%) and negative predictive value of 90.5% (95% CI 69.6% to 98.8%).

Simplification of the model: the nomogram. Based on our data set, we varied the value of NYHA functional class from I to IV and LAT area from 0.5 to 12.5 cm^2. A nomogram presenting a line graph for each NYHA functional class was constructed (Fig. 2). A horizontal line corresponding to P = 0.7 indicates the optimal cut-off point that maximizes the diagnostic performance of the model.

DISCUSSION

Percutaneous transvenous mitral commissurotomy has been accepted as a safe and effective alternative treatment to surgery, and it results in a good immediate hemodynamic outcome, a low complication rate and sustained hemodynamic and clinical improvement in the majority of symptomatic patients with mitral stenosis (1–10). The presence of LAT, however, is generally considered a contraindication to this procedure, leaving the open surgical commissurotomy the only treatment option. The reported incidence of LAT in rheumatic mitral stenosis is between 10% and 25% (27), as compared with 22% in our study.

Surgical repair of mitral stenosis. In our institution, the waiting list for mitral valve surgery for patients with severe mitral stenosis is approximately 9 to 15 months, and during that time, patients must be given oral anticoagulant therapy to prevent thromboembolic events. If the probability of LAT disappearance in a particular patient was known, only those patients needing surgical repair would be put on the waiting list, thus allowing those in greatest need to move up the queue, saving resources and precluding serious complications. We have tried to achieve this goal by using the data available in our setting, albeit from a small sample.

Variables of the prognostic model. Atrial fibrillation and left atrial size were not statistically significant independent variables. However, the higher the NYHA functional class, the less likely the LAT was to disappear. The pathophysiology of thrombogenesis in congestive heart failure could be

Table 5. The Final Model

Variables	Coefficient	Standard Error	OR	95% CI	p Value
NYHA (one-class increase)	−1.8012	0.7267	0.16	0.04–0.69	0.013
LAT area (1-cm^2 increase)	−0.7028	0.2384	0.49	0.31–0.79	0.003
Constant	8.0827	2.3242	—	—	—

Abbreviations as in Table 2.

JACC Vol. 39, No. 5, 2002
March 6, 2002:886–91

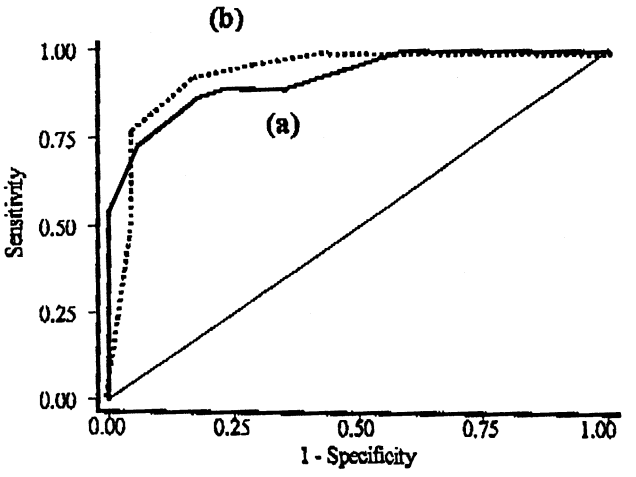

Figure 1. Receiver-operating characteristics (ROC) curves for prediction model derived from **(a)** the training set (**solid line**; area under the ROC curve = 0.92) and **(b)** the validating set (**dotted line**; area under the ROC curve = 0.94). Test for equivalence of the two area under the ROC curves, p = 0.462.

explained by Virchow's original triad of low cardiac output, aberrant flow through a dilated cardiac chamber or poor contractility, which all produce "flow abnormalities" that predispose to intracardiac thrombus formation (28). In patients with mitral stenosis who have a higher NYHA functional class, or clinically congestive heart failure, the severe "stasis" of blood within a dilated left atrial chamber may reflect not only the higher risk toward thrombus formation, but also the less likelihood of thrombus resolution.

During the follow-up period of 34 months (median 12.2), there were no losses. However, the information on time was not fully utilized by our logistic regression. Our model predicted a 34-month outcome of oral anticoagulant therapy for LAT resolution, but the chance of such an outcome occurring might not be constant over the entire follow-up period. Cox regression analysis, which might yield a prognostic probability of the outcome at a specified point in time, was not considered, because we aimed for a simple and easy-to-understand model. Instead, we used multiple logistic regression analysis and the ROC curve to estimate the diagnostic performance, including sensitivity, specificity and predictive values, similar to a conventional two-by-two table, as used by most clinicians.

Clinical implications of the model. The clinical judgment of the care provider, regarding the need for surgery, is usually valid in obvious cases. For example, patients with NYHA functional class IV or a large LAT size should have an immediate operation. For a large proportion of the patients, however, surgical repair was uncertain. The model could be used to decide which patients should get priority for surgery and which ones might have LAT resolution, as well as the chance of each. Clinicians can also use the nomogram (Fig. 2) as a consultation tool for their patients.

The nomogram can be applied once the NYHA functional class and LAT area of the patient are known. For example, a patient with an LAT area of 7 cm^2 and NYHA functional class I will have an 80% chance of LAT resolution. However, patients in class IV will have a very small chance of LAT resolution, no matter how small the LAT area; this type of patient needs immediate surgery.

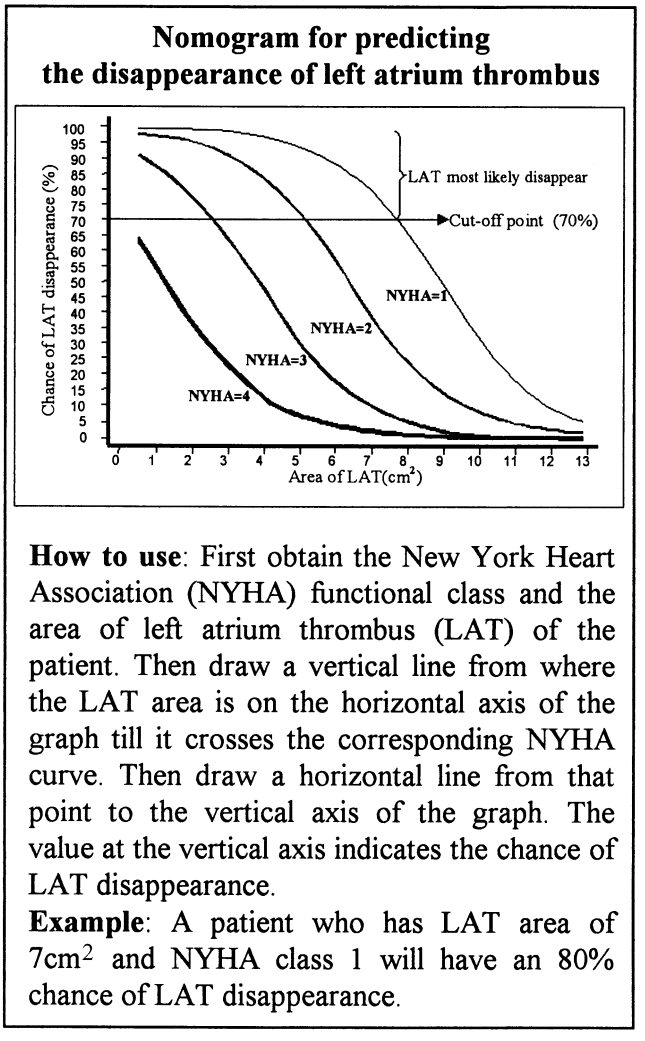

Figure 2. Nomogram for predicting the disappearance of LAT.

Advantage of the model. This prognostic model includes only two variables to derive a risk score. It is simple and highly predictive. To the best of our knowledge, this is the first predictive model for this type of patient. Our model was developed using a data set, and it was validated and confirmed by another data set, ensuring its validity (29,30). However, our validating cohort was a subset of the study group using the same health care facilities as the training one. Further validating studies in different health care settings are needed to confirm this prognostic tool.

Study limitations. Although this study included the largest set of PTMC candidates with LAT ever reported, the sample size is still rather small, specifically concerning the outcomes of interest. This could have resulted in a lack of

association with some potentially important variables in LAT resolution. We would need a larger sample to demonstrate their association with the disappearance of LAT. Notwithstanding, our aim was to find a simple predictive model; one with few variables and a high accuracy of prediction is preferable, even if some potential risk factors were consequently excluded. Moreover, we also tried to limit the number of variables before seeing the results, to avoid over-fitting the model.

It should also be emphasized that patient compliance (maintaining the therapeutic dosage of INR) may play an important role in LAT resolution.

Conclusions. We have derived, checked and externally validated a prognostic model for predicting LAT resolution among PTMC candidates receiving long-term oral anticoagulant therapy. The final model achieves a highly predictive accuracy, requires an easily measurable set of clinical and TEE findings and can be applied using a simple nomogram in the medical department of any hospital equipped with an echocardiograph. Although such a model cannot replace clinical judgment, it helps both physicians and patients to make better decisions. To confidently recommend its use, the establishment of its use in different health care settings is advised.

Acknowledgments

The authors thank Mr. Bryan Roderick Hamman for assistance in preparing the manuscript. We also thank the patients for their participation and the colleagues, nurses and other staffs of the hospital who cared for patients with PTMC. We are grateful to the many doctors who referred patients to us.

Reprint requests and correspondence: Dr. Songkwan Silaruks, Department of Medicine, Faculty of Medicine, Khon Kaen University, Mitrapap Road, Khon Kaen, 40002, Thailand. E-mail: songkw-s@medlib2.kku.ac.th.

REFERENCES

1. The National Heart, Lung, and Blood Institute Balloon Valvuloplasty Registry Participants. Multicenter experience with balloon mitral commissurotomy: NHLBI Balloon Valvuloplasty Registry report on immediate and 30-day follow-up results. Circulation 1992;85:448–61.
2. Inoue K, Owaki T, Nakamura T, Kitamura F, Miyamoto N. Clinical application of transvenous mitral commissurotomy by a new balloon catheter. J Thorac Cardiovasc Surg 1984;87:394–402.
3. Vahanian A, Michel PL, Cormier B, et al. Results of percutaneous mitral commissurotomy in 200 patients. Am J Cardiol 1989;63:847–52.
4. Abascal VM, O'Shean JP, Wilkins GT, et al. Prediction of successful outcome in 130 patients undergoing percutaneous balloon mitral valvulotomy. Circulation 1990;82:448–56.
5. Rediker DE, Block PC, Abascal VM, et al. Mitral balloon valvuloplasty for mitral restenosis after surgical commissurotomy. J Am Coll Cardiol 1988;2:252–6.
6. Palacios IF, Block PC, Wilkins GT, et al. Follow-up of patients undergoing percutaneous mitral balloon valvotomy: analysis of factors determining restenosis. Circulation 1989;79:573–9.
7. Block PC, Palacios IF, Block EH, et al. Late (two year) follow-up after percutaneous mitral balloon valvotomy. Am J Cardiol 1992;69:537–41.
8. Nobuyoshi M, Hamasaki N, Kimura T, et al. Indications, complications, and short-term clinical outcome of percutaneous transvenous mitral commissurotomy. Circulation 1989;80:782–92.
9. Chen CR, Cheng TO, Chen JY, et al. Percutaneous mitral valvuloplasty with the Inoue balloon catheter. Am J Cardiol 1992;70:1455–8.
10. Hung JS, Chern MS, Wu JJ, et al. Short- and long-term results of catheter balloon percutaneous transvenous mitral commissurotomy. Am J Cardiol 1991;67:854–62.
11. Tsai LM, Hung JS, Chen JH, et al. Resolution of left atrial appendage thrombus in mitral stenosis after warfarin therapy. Am Heart J 1991;121:1232–4.
12. Pytlewski G, Panidis IP, Combs W, et al. Resolution of left atrial thrombus with warfarin by transesophageal echocardiography before percutaneous commissurotomy in mitral stenosis. Am Heart J 1994; 128:843–5.
13. Kang DH, Song JK, Chae JK, et al. Comparison of outcomes of percutaneous mitral valvuloplasty versus mitral valve replacement after resolution of left atrial appendage thrombi by warfarin therapy. Am J Cardiol 1998;81:97–100.
14. Hung JS, Lin FC, Chiang CW. Successful percutaneous transvenous catheter balloon mitral commissurotomy after warfarin therapy and resolution of left atrial thrombus. Am J Cardiol 1989;64:126–8.
15. Alfonso F, Garcia-Fernandez MA, Sanz A, et al. Disappearance of a thrombus in the left atrial appendage after treatment with Coumadin: a two-dimensional echocardiographic study. Am J Noninvas Cardiol 1992;6:66–8.
16. The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis, 9th ed. Boston, MA: Little, Brown and Company, 1994, 143–9.
17. Wilkins GT, Weyman AE, Abascal VM, Block PC, Palacios IF. Percutaneous mitral valvotomy: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. Br Heart J 1988;60:299–308.
18. Feigenbaum H. Echocardiography. 4th ed. Philadelphia, PA: Lea & Febiger, 1986;592–9.
19. Fatkin D, Kuchar DL, Thorburn CW, et al. Transesophageal echocardiography before and during direct current cardioversion of atrial fibrillation: evidence for 'atrial stunning' as a mechanism of thromboembolic complications. J Am Coll Cardiol 1994;23:307–16.
20. Hirsh J, Dalen JE, Anderson DR, et al. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. Chest 1998;114:445S–69S.
21. Harrell FE, Lee KL, Mark DB. Tutorial in biostatistics: multivariable prognostic models—issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med 1996;15:367–87.
22. Kleinbaum DG, Kupper LL, Muller KE, et al. Applied regression analysis and other multivariable methods. Pacific Grove, CA: Duxbury Press, 1998;386–409.
23. Hosmer DW, Lemeshow S. Applied Logistic Regression. New York, NY: John Wiley & Sons, 1989;135–71.
24. Goldstein R. Srd15: restricted cubic spline functions. Newton HJ, ed. The Stata Technical Bulletin Reprints, Vol. 2. College Station, TX: Stata Corporation, 1992.
25. Hanley JA, McNeil BJ. The meaning and use of the area under the receiver operating characteristics (ROC) curve. Radiology 1982;143: 29–36.
26. Cleves M. Sg120: receiver operating characteristics (ROC) analysis. Newton HJ, ed. The Stata Technical Bulletin Reprints, Vol. 9. College Station, TX: Stata Corporation, 2000.
27. Schrestha NK, Moreno FL, Narcico FV, Torres L, Calleja HB. Two-dimensional echocardiographic diagnosis of left atrial thrombus in rheumatic heart disease: a clinicopathologic study. Circulation 1983;67:341–7.
28. Lip GYH, Gibbs CR. Does heart failure confer a hypercoagulable state? Virchow's triad revisited. J Am Coll Cardiol 1999;33:1424–6.
29. Wyatt JC, Altman DG. Commentary on prognostic models: clinically useful or quickly forgotten? BMJ 1995;311:1539–41.
30. Altman DG, Royston P. What do we mean by validating a prognostic model? Stat Med 2000;19:453–73.